REMARKS

Claims 48, 50, 52-61, and 63-68 appear in this application for the Examiner's review and consideration.

Claim 50 has been amended to recite proper dependency on independent claim 48. Claim 60 and 61 have been amended, as suggested by the Examiner, to more clearly recite alternative dependency on claims 54-59. Claim 65 has been amended to delete the pharmaceutical carrier. No new matter has been added by any of theses amendments. No fee is believed due for these amendments.

The Rejections Under § 112 Has Been Obviated

Claim 65 was rejected on Pages 2-3 of the Office Action under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Examiner alleges that the term "elixir" is synonymous with "pharmaceutically acceptable carrier or excipient." Applicants have deleted the phrase "pharmaceutically acceptable carrier or excipient" in order to expedite allowance of the application. This amendment renders the rejection of the carrier unnecessary and thus obviates the rejection.

Claim 50 was rejected on Page 3 of the Office Action as lacking antecedent basis because it depended from a canceled claim. Claim 50 has been amended to recite proper dependency from pending independent claim 48.

For the above reasons, the rejections of claims 50 and 65 under 35 U.S.C. § 112, second paragraph, should be withdrawn.

The Rejections Under § 102 Have Been Obviated

Claims 48, 50, 52-54, 60, 61, and 63-65 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 4,659,716 to Villani *et al.* ("Villani") for the reasons set forth on pages 3-5 of the Office Action. Applicants respectfully traverse this rejection for the reasons provided below.

It is settled law that a prior art reference must disclose all the elements of a claim in order to anticipate the invention recited by that claim. *See* M.P.E.P. §2131. There must be no difference between the claimed invention and the reference disclosure as viewed

by one of ordinary skill in the art. *See Scripps Clinic & Research Fdn. v. Genentech*, 927 F.2d 1565, 1576 (Fed. Cir. 1991). Put another way, "[a] claim is anticipated and therefore invalid only when a single prior art reference discloses *each and every limitation of the claim.*" *Glaxo Inc. v. Novapharm Ltd.*, 52 F.3d 1043, 1047, *cert. denied*, 116 S. Ct. 516 (1995) (citations omitted) (emphasis added).

Villani discloses a general class of compounds, 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines. Villani, col. 1, lines 17-38. But while Villani suggests pharmaceutical compositions containing these compounds, it does not disclose even one pharmaceutical composition that *specifically* contains descarboethoxyloratidine ("DCL"). *See, e.g.*, Villani, Col. 1, lines 43-45; Col. 8, lines 44-46. Villani merely generically discloses that the 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines or can be formulated into pharmaceutical compositions alone or with therapeutic agents. However, Villani does not disclose a pharmaceutical composition comprising the specific compound DCL, much less DCL and a decongestant, as recited by claims 48, 50, and 52-53. Villani merely mentions that pharmaceutical preparations can be made which comprise "from 1 mg to 1000 mg" of an "active compound" which can "also contain other therapeutic agents, such as decongestants." Villani, Col. 8, lines 42-46. Applicants respectfully submit that this disclosure is insufficient to render the claims anticipated under 35 U.S.C. § 102(b).

Claims 48, 50, and 52-53 recite, in part, pharmaceutical compositions that comprise from about 0.1 mg to about 5 mg DCL and an amount of decongestant. Villani clearly does not anticipate the claimed invention for at least two reasons. First, Villani fails to specifically disclose *any* pharmaceutical compositions comprising DCL, much less a pharmaceutical composition comprising DCL and a decongestant. Second, the amount of DCL recited by claim 48 is drastically less than that which is at best only suggested by Villani. Indeed, Villani suggests a maximum amount of an "active ingredient" which is *200 times* greater than that recited by claim 48. Further, only about the bottom 1% of the range suggested by Villani overlaps with that recited by amended claim 48. Consequently, Applicants respectfully submit that the claimed amount of DCL is not disclosed with sufficient specificity by Villani to read on an element of the claimed invention.

Independent claim 54 recites a pharmaceutical composition that comprises DCL, or a pharmaceutical salt thereof, pseudoephedrine, and a pharmaceutically acceptable carrier. Villani, however, only suggests that pharmaceutical compositions can be formulated to contain a 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta- [1,2-b]pyridine and another "therapeutic agent, such as decongestants." Villani, col. 8, lines 42-46. Villani does not disclose a specific pharmaceutical composition comprising DCL. Villani further does not disclose a single specific decongestant, much less pseudoephedrine. Therefore, Villani cannot anticipate a pharmaceutical composition specifically containing DCL and pseudoephedrine.

Furthermore, it is well established law that prior art is anticipatory only if every element of the claimed invention is disclosed in a single item of prior art in the form literally defined in the claim. *See Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); *Jamesbury Corp. v. Litton Indus. Products*, 756 F.2d 1556 (Fed. Cir. 1985); *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 USPQ 409 (Fed. Cir. 1984). If it is necessary to rely upon a second item of prior art to combine with the principal item of prior art in order to complete the teaching of the claim, then the combination of these references will not constitute a § 102 anticipation. *See Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264 (Fed. Cir. 1991).

However, the Examiner insists on using a combination of Villani and The Merck Manual, 16th Ed., Merck Research Laboratories, 326-332 and 2345-2346 (1992) ("Berkow") to anticipate the pending claims. Applicants respectfully submit that such a combination is deemed improper under 35 U.S.C. §102(b) because the second reference is cited to fill in the limitation that is missing from an anticipatory reference. Legally, this is improper. For these reasons, Applicants respectfully submit that the invention as recited by the pending claims is not anticipated by Villani. Applicants further submit that because the ranges of "active ingredient" disclosed by Villani do not even remotely disclose the amount of DCL recited by dependent claim 60, the rejection of claims 60-61 under § 102 should also be withdrawn.

The Rejections Under §103 Have Been Obviated

Claims 48, 50, 52-54, 60, 61, and 63-65 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Villani and Berkow for the reasons set forth on pages 5-6 of the Office Action. Applicants respectfully traverse this rejection.

As the Examiner is well aware, three basic criteria must be met to establish a case of *prima facie* obviousness: first, there must have been at the time of the invention a motivation to combine the references cited; second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious; and third, there must have been at the time of the invention a reasonable expectation of success. MPEP § 2142. It is further well settled that the disclosure of a genus does not by itself render obvious a species within that genus, and that absent the further teaching or suggestion of a specific composition, the disclosure of a large genus of compounds does render obvious a specific composition comprising one of them. *See, e.g.*, MPEP § 2144.08; *In re Baird*, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994); *In re Jones*, 21 U.S.P.Q.2d 1941, 1943 (Fed. Cir. 1992).

Villani discloses a class of compounds, 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines. Villani, col. 1, lines 17-38. As is readily apparent to those skilled in the art, Villani discloses at least over 100 individual compounds. Further, Villani only generally discloses pharmaceutical compositions comprising any one of 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines in an *unspecified amount* ranging from 1 mg to 1000 mg in optional combination with a second "therapeutic agent," such as a decongestant. Villani, col. 8, lines 42-47. In stark contrast, the claimed invention relates to a particular combination of specific compounds in specific amounts for a specific purpose such that a broad generic disclosure is not legally sufficient to render the species *prima facia* obvious. *See In re Baird* 16 F.3d 380 (Fed. Cir. 1994). *See also In re Jones* 958 F.2d 347 (Fed. Cir. 1992).

Berkow merely discloses an antihistamine-decongestant composition containing the decongestant pseudoephedrine. Berkow, page 326. Berkow does not disclose a specific antihistamine, much less a non-sedating antihistamine, such as DCL.

Claim 48 recites a pharmaceutical composition that comprises from about 0.1 mg to about 5 mg of DCL and an amount of decongestant. This composition is clearly not rendered obvious by Villani alone or in combination with Berkow.

Villani does not disclose or suggest a pharmaceutical composition comprising the *specific* compound DCL, which is only one of the many species encompassed by the genus disclosed by Villani, and a decongestant. Only with the aid of impermissible hindsight can the specific combination of DCL and a decongestant be identified from the broad disclosure that a 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridine can be combined with another "therapeutic agent." Applicants further submit that even in combination with Berkow, Villani provides no suggestion of a pharmaceutical composition comprising DCL and pseudoephedrine, much less the required reasonable expectation of success. This is because, assuming *arguendo* that there is motivation to combine them, the combination of the two references suggests only that one of ordinary skill in the art try a pharmaceutical composition comprising pseudoephedrine and one of the over 100 compounds disclosed by Villani. As the Examiner is aware, "obvious to try" is not the proper standard. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F2d 1367, 1380 (Fed. Cir. 1986). Therefore, the claimed invention is not rendered obvious.

The invention as now recited by the pending claims is further not obvious over Villani alone or in combination with Berkow because neither reference provides a suggestion of a pharmaceutical composition comprising the specific compound DCL in an amount of from about 0.1 mg to about 5 mg. Indeed, by suggesting a range of "active ingredient" of from 1 mg to 1000 mg (col. 8, lines 42-47), and by providing only examples wherein the amount of the single active ingredient is either 100 mg or 500 mg (*see, e.g.*, col. 22, lines 39 and 63), Villani teaches away from the small amounts of DCL that are combined with another active ingredient as recited by the claims. Consequently, at the time of this invention, one skilled in the art would have had no motivation to make, much less a reasonable expectation that compositions comprising such small amounts of one specific compound within the large genus disclosed by Villani would have any usefulness when combined with a decongestant.

Finally, as recognized by the Examiner on Pages 5-6 of the Office Action, Villani "does not disclose pharmaceutical compositions wherein a specific decongestant has been specified." The Examiner further states, Berkow "does not disclose pharmaceutical compositions wherein DCL and any one decongestant have been specified as the active ingredients." Thus, because Villani does not disclose a pharmaceutical composition containing DCL as recited by the claims or disclose a specific decongestant, and because

Berkow does not disclose DCL or a specific decongestant as claimed, one of ordinary skill in the art would clearly have no motivation to combine the cited references as is implied from the Examiner's statements in the Office Action. Assuming *arguendo* that there was a motivation to combine, one of ordinary skill in the art, absent the impermissible use of hindsight, would clearly not arrive at the claimed invention.

In sum, neither Villani nor Berkow suggest DCL in an amount of from about 0.1 mg to about 5 mg and a decongestant, such as pseudoephedrine, much less provide the required reasonable expectation of successfully arriving at the claimed invention. Applicants thus respectfully request that the rejection of claims 48, 50, 52-54, 60-61, and 63-65 under § 103 be withdrawn.

Claims 55-61 and 66-68 were rejected under 35 U.S.C. §103(a) as being unpatentable over Villani and Remington's Pharmaceutical Sciences, 18th Ed., Philadelphia College of Pharmacy and Science, 1097-1130 (1990) ("Gennaro") for the reasons set forth on pages 6-8 of the Office Action. Applicants respectfully traverse this rejection.

Villani discloses "other therapeutic agents" which encompass an undisclosed and a vast, if not infinite, number of compounds. However, Villani does not specifically disclose non-steroidal anti-inflammatory agents or non-steroidal analgesics, much less disclose a specific example of either.

Genarro discloses pharmaceutical compositions containing antihistamines and mild analgesics. Particularly, Genarro discloses only combinations of first generation antihistamines, known to cause sedation and other adverse-effects, with mild analgesics. *See* Page 1131, Col. 2. Genarro fails to disclose any second generation, non-sedating antihistamines, much less to specifically disclose DCL. *See* Specification at Page 7, line 34 to Page 8, line 3. Genarro also fails to specifically disclose combinations of DCL and a non-steroidal anti-inflammatory agent or non-narcotic analgesic.

Claims 55-61 and 66-68 recite pharmaceutical compositions comprising DCL and a specific non-steroidal anti-inflammatory agent or non-narcotic analgesic. These compositions are clearly not rendered obvious by Villani alone or in combination with Genarro for the following reasons. Villani provides no disclosure or suggestion of a pharmaceutical composition comprising the *specific* compound DCL, which is only one of the many species encompassed by the genus disclosed by Villani, and a non-steroidal anti-inflammatory agent or non-narcotic analgesic. Further, when combined with the at least one

hundred 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines disclosed by Villani, the vast, if not infinite, number of "other therapeutic agents" does not even remotely suggest the specific combination of DCL and a non-steroidal anti-inflammatory agent or non-narcotic analgesic, as claimed herein. Indeed, Applicants respectfully submit that only with the aid of impermissible hindsight can the specific combination of DCL and a non-steroidal anti-inflammatory agent or non-narcotic analgesic be identified from the general disclosure that a 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridine can be combined with another "therapeutic agent." For this reason, Applicants further submit that even in combination with Genarro, Villani provides no suggestion of a pharmaceutical composition comprising DCL and a non-steroidal anti-inflammatory agent or non-narcotic analgesic, as recited by claims 66-68, much less a pharmaceutical composition comprising DCL and the specific non-steroidal anti-inflammatory agents or non-narcotic analgesics recited by claims 55-61. This is because, assuming *arguendo* that there is a motive to combine, the combination of the two references suggests only that one of ordinary skill in the art try a pharmaceutical composition comprising a mild analgesic and one of the vast number of compounds disclosed by Villani. At best, Villani and Genarro render the combination of DCL and a non-steroidal anti-inflammatory "obvious to try." This is not, however, the proper test of obviousness. *Hybritech*, 802 F2d at 1380. Thus, the combination of Villani and Genarro does not suggest the claimed invention, much less provide a reasonable expectation of success. Further, the combination of Villani and Genarro requires one of ordinary skill in the art to impermissibly "pick and choose" DCL of Villani and an analgesic of Genarro, which is only possible when using the present claims as a blueprint, which is improper. Thus, the combination of Villani and Genarro cannot obviate the pending claims since one of ordinary skill in the art would clearly have no reasonable expectation of success. For all the above reasons, Applicants respectfully request that the rejection of claims 55-61 under U.S.C. § 103(a) be withdrawn.

Conclusion

Applicants respectfully request the entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all pending claims are now in condition for allowance. Should any additional fees be due, please charge all such fees to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date: April 4, 2001

45,479
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Enclosures

A copy of the marked up amendments to the title (Exhibit A)

APPLICATION NO. 09/039,260 DOCKET NO. 4821-306

(As amended under 37 C.F.R. § 1.116; April 4, 2001)

50. (Twice Amended) The pharmaceutical composition of [claim 49] claim 48 wherein the amount of descarboethoxyloratadine is from about 0.2 mg to about 1 mg.

60. (Amended) The pharmaceutical composition of any of claims 54, 55, 56, 57, 58 or 59 wherein said DCL is present in an amount from about 0.1 mg to about 10 mg.

61. (Amended) The pharmaceutical composition of any of claims [claim] 54, 55, 56, 57, 58 or 59 wherein said composition is adapted for oral delivery.

65. (Amended) An elixir which comprises an amount of descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof[,] and an amount of a decongestant[, and a pharmaceutically acceptable carrier].

A copy of the pending claims (Exhibit B)

APPLICATION NO. 09/039,260 DOCKET NO. 4821-306

(As amended under 37 C.F.R. § 1.116; April 4, 2001)

48. (Amended) A pharmaceutical composition which comprises from about 0.1 mg to 5 mg of descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier.

50. (Twice Amended) The pharmaceutical composition of claim 48 wherein the amount of descarboethoxyloratadine is from about 0.2 mg to about 1 mg.

52. The pharmaceutical composition of claim 48 wherein said composition is adapted for oral delivery.

53. The pharmaceutical composition of claim 48 wherein said composition is adapted for parenteral, rectal or transdermal delivery.

54. (Amended) A pharmaceutical composition which comprises from about 0.1 mg to 5 mg descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, pseudoephedrine, and a pharmaceutically acceptable carrier.

55. (Amended) A pharmaceutical composition which comprises descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, acetylsalicylic acid, and a pharmaceutically acceptable carrier.

56. (Amended) A pharmaceutical composition which comprises descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, acetaminophen, and a pharmaceutically acceptable carrier.

57. (Amended) A pharmaceutical composition which comprises from about 0.1 mg to 5 mg descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, ibuprofen, and a pharmaceutically acceptable carrier.

58. (Amended) A pharmaceutical composition which comprises descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, ketoprofen, and a pharmaceutically acceptable carrier.

59. (Amended) A pharmaceutical composition which comprises descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, naproxen, and a pharmaceutically acceptable carrier.

60. (Amended) The pharmaceutical composition of claims 54, 55, 56, 57, 58 or 59 wherein said DCL is present in an amount from about 0.1 mg to about 10 mg.

61. (Amended) The pharmaceutical composition of claim 54, 55, 56, 57, 58 or 59 wherein said composition is adapted for oral delivery.

63. A pharmaceutical composition which comprises from about 0.2 mg to about 1 mg of descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier.

64. An aerosol spray which comprises an amount of descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier.

65. (Amended) An elixir which comprises an amount of descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof and an amount of a decongestant.

66. A pharmaceutical composition which comprises from about 0.1 mg to 5 mg descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, a non-steroidal anti-inflammatory agent, and a pharmaceutically acceptable carrier.

67. A pharmaceutical composition which comprises descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, a non-narcotic analgesic, and a pharmaceutically acceptable carrier.

68. The pharmaceutical composition of claim 66 or 67 wherein the amount of descarboethoxyloratadine is from about 0.2 mg to about 1 mg.